

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application. All amendments are made without prejudice or disclaimer.

Listing of Claims

1. (Currently Amended) An isolated cross-reactive antibody or a fragment thereof, which specifically inhibits or blocks the mammalian Toll-like Receptor 2 (TLR2)-mediated immune cell activation by specifically binding to the C-terminal portion of the extracellular domains of at least human and murine TLR2, wherein the antibody or fragment thereof specifically binds through the variable regions of the heavy and light chains, wherein the heavy chain variable region comprises a complementarity determining region 1 (CDR1) region comprising the amino acid sequence Gly-Phe-Thr-Phe-Thr-Thr-Tyr-Gly (residues 58-64 of SEQ ID NO:46), a CDR2 region comprising the amino acid sequence Ile-Tyr-Pro-Arg-Asp-Gly-Ser-Thr (residues 83-90 of SEQ ID NO:46) and a CDR3 region comprising the amino acid sequence Ala-Arg-Leu-Thr-Gly-Gly-Thr-Phe-Leu-Asp-Tyr (residues 129-139 of SEQ ID NO:46), and wherein the light chain variable region comprises a CDR1 region comprising the amino acid sequence Glu-Ser-Val-Glu-Tyr-Tyr-Gly-Thr-Ser-Leu (residues 46-56 of SEQ ID NO:47), a CDR2 region comprising the amino acid sequence Gly-Ala-Ser (residues 74-76 of SEQ ID NO:47) and a CDR3 region comprising the amino acid sequence Gln-Gln-Ser-Arg-Lys-Leu-Pro-Trp-Thr (residues 113-121 of SEQ ID NO:47).

2. (Currently Amended) The antibody or antibody fragment of claim 1, wherein the antibody is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, a humanised antibody, a chimeric antibody, ~~or~~ and a synthetic antibody.

3. (Currently Amended) The antibody or antibody fragment of claim 1 or 2, wherein the antibody or fragment thereof specifically binds through the variable regions of the heavy chain

comprising the amino acid sequence as depicted in SEQ ID NO:6 and the light chain comprising the amino acid sequence as depicted in SEQ ID NO:7.

4. (Previously Presented) The antibody of claim 1, wherein said antibody is linked to a pharmaceutical agent, to a detectable agent, or both.

5. (Currently Amended) An isolated nucleic acid coding for the variable region[s] of the heavy chain of the antibody of claim 3, the light chain of the antibody of claim 3, or both.

6. (Previously Presented) An isolated nucleic acid which comprises the sequence of SEQ ID NO:1, SEQ ID NO:2, or both.

7. (Currently Amended) An isolated nucleic acid, which comprises ~~one or more~~ nucleic acids ~~selected from~~ Nos. 172-201, 244-294, and 385-417 of SEQ ID NO:1[~~;~~]; nucleic acids Nos. 130-174, 220-240 and/or 337-363 of SEQ ID NO:2; or both nucleic acids Nos. 172-201, 244-294 and 385-417 of SEQ ID NO:1 and nucleic acids Nos. 130-174, 220-240 and 337-363 of SEQ ID NO:2.

8. (Currently Amended) The isolated nucleic acid of one ~~or more~~ of claims 5-7, said isolated nucleic acid further comprising a nucleic acid encoding one or more regulatory sequences operably linked thereto.

9. (Previously Presented) A vector, which comprises the nucleic acid sequence of claim 5.

10. (Previously Presented) The vector of claim 9, which is an expression vector and which further comprises one or more regulatory sequences operably linked to said nucleic acid.

11. (Currently Amended) The vector of claim 9 or 10, ~~which is~~ wherein the vector is a plasmid or a retroviral vector.

12. (Previously Presented) An isolated host cell, which has been transformed with the vector of claim 9.
13. (Previously Presented) The isolated host cell of claim 12, which is a eukaryotic cell.
14. (Currently Amended) The isolated host cell of claim 13, wherein the cell is selected from the group consisting of a mammalian cell, a plant cell, a yeast cell ~~or~~ and an insect cell.
15. (Currently Amended) The isolated host cell of claim 14, wherein the cell is a mammalian cell selected from the group consisting of a CHO cell, a COS cell, a HeLa cell, a 293T cell, a HEH cell ~~or~~ and a BHK cell.
16. (Previously Presented) The isolated host cell of claim 12, wherein the cell is a prokaryotic cell.
17. (Previously Presented) The isolated host cell of claim 16, wherein the prokaryotic cell is *E. coli* or *Bacillus subtilis*.
18. (Currently Amended) A pharmaceutical composition comprising the antibody or antibody fragment thereof of claim 1, ~~a nucleic acid encoding the variable regions of the heavy and/or light chains of said antibody, or a vector comprising said nucleic acid and a~~ pharmaceutically acceptable carrier.
19. (Previously Presented) The pharmaceutical composition of claim 18, which further contains one or more pharmaceutically active ingredients.
20. (Previously Presented) The pharmaceutical composition of claim 18 or 19, wherein the one or more pharmaceutically active ingredients are selected from the group consisting of

antibiotic agents, anti-inflammatory agents, and agents which block a pattern recognition receptor.

21. (Previously Presented) The pharmaceutical composition of claim 20, wherein the pattern recognition receptor is selected from the group consisting of Toll-like Receptor 3 (TLR3), Toll-like Receptor 4 (TLR4), Toll-like Receptor 5 (TLR5), Toll-like Receptor 7 (TLR7), Toll-like Receptor 8 (TLR8) and Toll-like Receptor 9 (TLR9).

22. (Previously Presented) A hybridoma which produces a monoclonal antibody according to claim 2.

23. (Currently amended) A method of preventing ~~and/or~~ treating a TLR2 mediated inflammation process in a mammal, comprising administering the antibody of claim 1 or a fragment thereof, ~~a nucleic acid encoding the variable regions of the heavy chain of said antibody, the light chain of said antibody, or both, or a vector comprising said nucleic acid, or a composition comprising any thereof,~~ and a pharmaceutically acceptable carrier to said mammal in an effective amount to prevent ~~and/or~~ treat said TLR2-mediated inflammation process.

24. (Currently Amended) The method of claim 23, wherein ~~the~~ an individual dose is administered to ~~a~~ the mammal, preferably a human, is of between 1 mg to 100mg/kg body weight.

25. (Previously Presented) The method of claim 24, wherein the individual dose is administered as a single dose to the mammal.

26. (Currently Amended) The method of claim ~~25~~4, wherein the individual dose is administered repeatedly to the mammal.

27. (Previously Presented) The method of claim 24, wherein the dose is between 10 to 60 mg/kg body weight.

28. (Previously Presented) The method of claim 24, wherein the dose is between 20 to 40 mg/kg body weight.

29. (Cancelled)

30. (Currently Amended) The method of claim 23, wherein the TLR2 mediated ~~process~~ inflammation is TLR2 mediated septic shock ~~selected from rheumatoid or vascular arthritis, inflammatory bowel disease.~~

31. (Cancelled)

32. (Currently Amended) The antibody or fragment thereof of claim 1 wherein the antibody comprises:

a heavy chain variable region having the amino acid sequence of SEQ ID NO:1 ~~NO:4~~ NO:6;

a light chain variable region having the amino acid sequence of SEQ ID NO:2 ~~NO:5~~ NO:7; or both.

33. (Currently Amended) The antibody fragment of claim 1 comprising complementarity determining regions (CDRs) of the heavy chain variable domain, wherein the CDR1 region comprises the amino acid sequence Gly-Phe-Thr-Phe-Thr-Thr-Tyr-Gly (residues 58-64 of SEQ ID NO:4 ~~6~~ 5), the CDR2 region comprises the amino acid sequence Ile-Tyr-Pro-Arg-Asp-Gly-Ser-Thr (residues 83-90 of SEQ ID NO:4 ~~6~~ 5) and the CDR3 region comprises the amino acid sequence Ala-Arg-Leu-Thr-Gly-Gly-Thr-Phe-Leu-Asp-Tyr (residues 129-139 of SEQ ID NO:4 ~~6~~ 5), and/or the complementarity determining regions (CDRs) of the light chain variable domain, wherein the CDR1 region comprises the amino acid sequence Glu-Ser-Val-Glu-Tyr-Tyr-Gly-Thr-Ser-Leu (residues 46-56 of SEQ ID NO:4 ~~7~~ 7), the CDR2 region comprises the amino acid

sequence Gly-Ala-Ser (residues 74-76 of SEQ ID NO:~~47~~) and the CDR3 region comprises the amino acid sequence Gln-Gln-Ser-Arg-Lys-Leu-Pro-Trp-Thr (residues 113-121 of SEQ ID NO:~~47~~).

34. (Currently Amended) The antibody fragment of claim 1 wherein the antibody fragment is selected from the group consisting of ~~a~~ Fab antibody fragment, a F(ab')₂ antibody fragment ~~or~~ and an Fv antibody fragment.

35. (Currently Amended) An isolated antibody encoded by the isolated nucleic acid of claim 6.